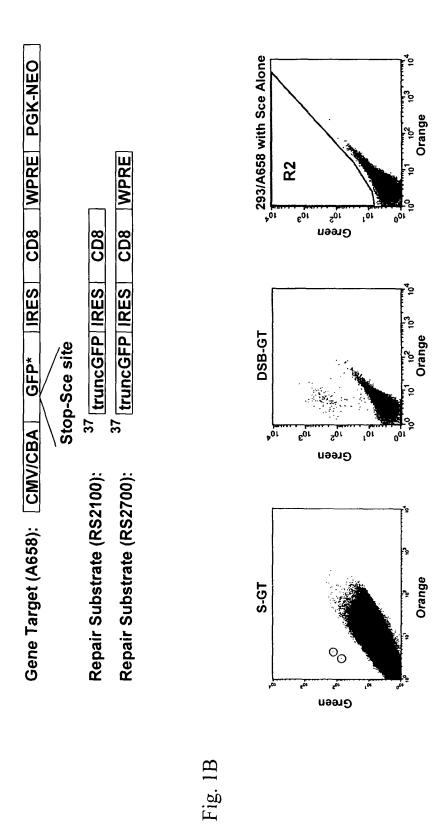
Fig. 1A



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Fig. 1C

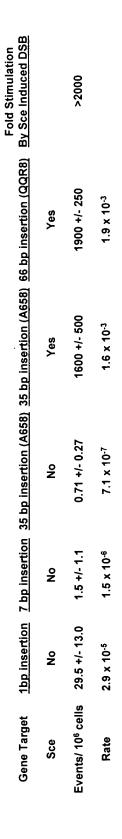
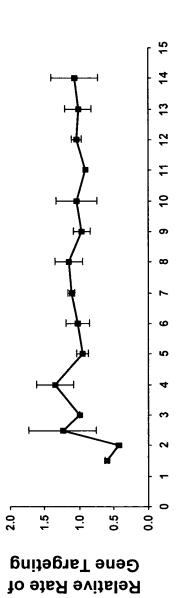
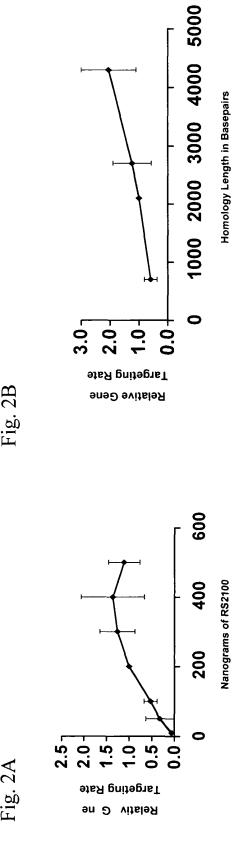


Fig. 1D



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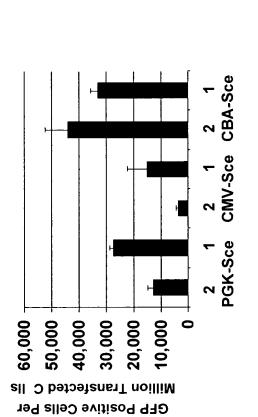


1.5 1.0 2.5 2.0 Targeting Rate Relative Gene Fig. 2D PGK-Sce 500 400 Nanograms of Sce Expression Plasmid CBA-Sce 300 200 100 3.0 2.5 1.5 1.0 0.5 Targeting Rate Relative Gen

Transcribed

Untranscribed

Fig. 2E



Chimeric Nucleases:

CMV-QQR-L18-Fn: CMV ATGN QQR L18 Nuclease QQR8: 5' GFP StopQQR Site 8 31S ADD Sce Site 3' GFP

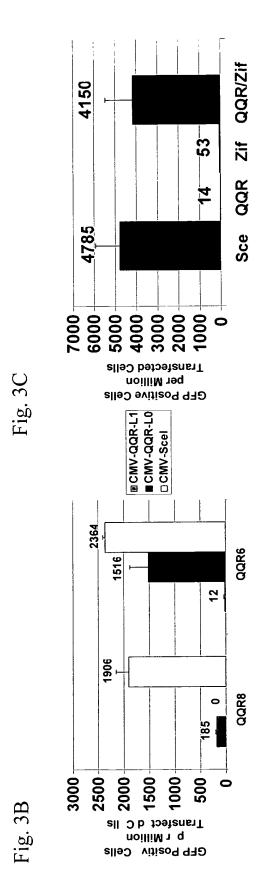
Targets:

QQR6:

CMV-QQR-L0-Fn: CMV ATGNQQR L0 Nuclease 5' GFP StopQQR Site eatis ADD Sce Site 3' GFP

CMV ATGN Zif L3 Nuclease CMV-Zif-L3-Fn: QQRZif6: 5' GFP StopQQR Site | 91!S JIZ | Sce Site 3' GFP





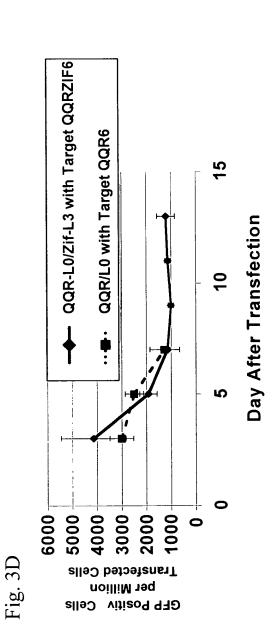


Fig. 4

Fn HBGZF2

Fn HBGZF4

act AGCAACCT Ca aacag ACACCAT GCt gcat ct gact cct gaggagaagt ct gcc GTTACT GCCct gt gg GGCAAGGT Gaacg tgaTCGTT GGACtt gt cTGT GGT ACCa cgt agact gaggact cct ctt cagacgg CAAT GAC GCgacacc CCGTT CCACt gc

HBGZF1 Fn

HBGZF3 Fn

Design of HBGZF1

Target Binding Site: 5' GAG GTT GCT 3' F3 F2 F1

-1 1 2 3 4 5 6 B3 B2 B1 Finger 1: GCT QSSDLT R TSGELVR GTT TSGALTR TSGSLTR

Finger 2

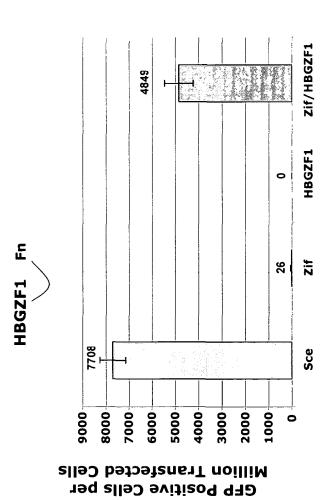
Finger 3: GAG RSDNLTR RSDNLVR

Structure of CMV-HBGZF1

ATG-NLS-FLAG-Finger 1(QSSDLTR)-Finger2(TSGALTR)-Finger3(RSDNLTR)-Fn

Gene Targeting with HBGZF1

Target: GFPStop AGCAACCTOt ct aga GCGT GGGCG Sce Ste GFP Fn ZIF268 TCGTT GGA Gagat d CGCACCCGC



Nuclease Transfected

Design of HBGZF4

Target Binding Site: 5' GGC AAG GTG 3'

F2 F3

-1 1 2 3 4 5 6 B3 B2 B1

Finger 1: GTG

DALT NSLT တ တ **~** ~

H nger 2 AAG

R S D T L S N R K D N L K N R S S N L T Q

Hnger 3: GGC

∢⊢∢>

DRSHL ESNHLT ERSKL/ DPGHL

Structure of CMV-HBGZF1

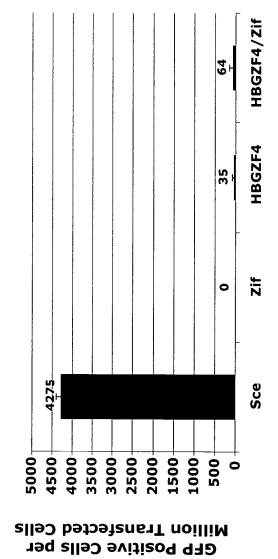
ATG-NLS-FLAG-Finger 1(RSDALTR)-Finger2(RSSNLTQ)-Finger3(DRSHLAR)-Fn

Gene Targeting with HBGZF4

Fn ZIF268

Target: GFP.St op. CACCTTGCCt daga GCGTGGGCG SceSte GFP GTGGAACGGagat ct CGCACCCGC

HBGZF4 Fn



Nuclease Transfected

Human Common Gamma Chain Deficiency

TM B	missense mutation	nonsense mutation	deletion frameshift	splice-site mutation		From Notarangelo et al. (2000)
\$ 68	0	•	◀	*		From No
	signal peptide	3' untranslated	conserved cysteine	WSXWS motif	ususmentivane domain	box1~box2 motaf
	<u> </u>		Ü	*	TS	

Fig. 9B

Exon 5

5 gaacaat cagt ggattatagacat aagtt ctt gcct agt gt ggat gggcagaaacgct acacgttt cgt gtt 3' ctt gtt agt cacct aatat ct gtatt caagaggaacggat cacacct acccgt cttt gcgat gt gcaaagcacaa WSXWS motif

cggagccgctttaacccactct ct ct ggaagt gct cagcatt ggact gaat ggagccacccaat ccact ggggggagca gcd cggcgaaaft gggt gagacacdt cacgagt cgt aacd cadtacd cggt gggtt aggt gaccccd cgt

atacttcaaaagag 3 tatgaagttttctg 5

Design of HCGCZF2

Target Binding Site: 5' GGG GGA GCA 3'

F2 F3

-1 1 2 3 4 5 6 B3 B2 B1

aaaa Finger 1: GCA

S L D L D L 0 0 0 z တတတ

民民民政

Finger 2 GGA

水 只 床 oш F QSGHL QRAHL QSSHL

H nger 3 GGG

 $\alpha \alpha \alpha$ S D H L S D H L S S H L ~ ~ ~

Structure of CMV-HCGCZF2

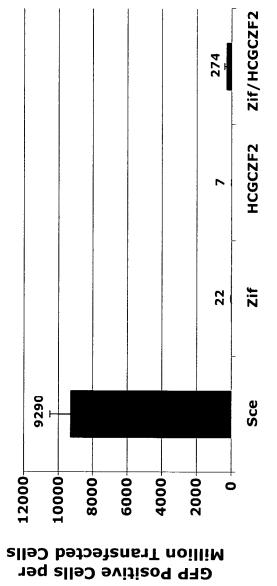
ATG-NLS-FLAG-Finger 1(QSNDLTR)-Finger2(QSSHLTR)-Finger3(RSSHLTR)-Fn

Gene Targeting with HCGCZF2

Fn ZIF268

Target: GFP Stop TGCTCCCCC ctaga GCGTGGGCG SceSte GFP ACGA GGGGagat ct CGCACCCGC

HCGCZF2 Fn



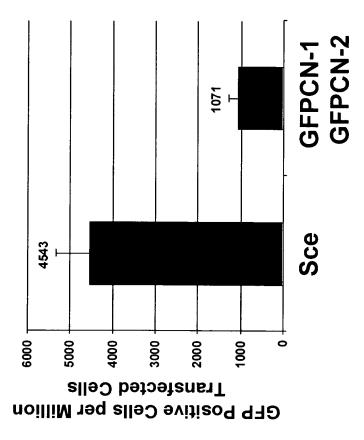
Nuclease Transfected

Fig. 12A

Fn GFPCN2

5 acC at CttCttc aag Gac Gac Ggc aac stop- Sce site tac 3' tgGtaGaaGaagttc Cgc Ctg Ccgttc

GFPCN1 Fn



Fn CD8ZF2

bp 441 5 acc ggCgcCcaC catcgc GcGcaGcc ctg 3 bp 471 tgg ccGcg Ggt G gtagcg Cag Cgt Cgg gac CD8ZF1、Fn

Fig. 13B

